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10/540,490	01/20/2006	Carmen Almansa Rosales	3494-107	3559

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EXAMINER	
SHIAO, REI TSANG	

ART UNIT	PAPER NUMBER
1626	

NOTIFICATION DATE	DELIVERY MODE
09/12/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/540,490	ALMANSA ROSALES ET AL.	
	Examiner	Art Unit	
	REI-TSANG SHIAO	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/07/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign application:

SPAIN P200202992 with a filing date 12/24/2002.

2. Claims 42-62 are pending in the application.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement filed on July 07, 2008 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Responses to Election/Restriction

4. Applicant's election with traverse of election of Group I claims 42-62, in part, in the reply filed on July 07, 2008 is acknowledged. Election of a compound N-[4-[4-chloro-5-(3-fluoro-4-methoxyphenyl)imidazol-1-yl]phenylsulfonyl]phosphoramidic acid as a single species is also acknowledged. The traversal is on the grounds that compounds of formula (I) do contain a novel common structure that constitutes a distinctive feature over the prior art, and applicants thus request that the compounds of at least Groups I and II be examined together. This is found persuasive, in part, and the reasons are given *infra*.

Claims 42-62 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 42-62, in part, drawn to compounds/compositions of formula (I), wherein the variable A represents imidazole, pyrazole, isoxazole or oxazole thereof, the variable D represents phenyl or pyridine thereof, the variables R1, L and B independently do not

represent heteroaryl, heterocycle or together form a ring moiety thereof, the variables R1, L and B independently are not substituted with heteroaryl, heterocycle thereof, and their methods of use.

The claims 42-62 herein lack unity of invention under PCT rule 13.1 and 13.2 since the compounds defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art, see Tawada et al. CAS: 139:246034. Tawada et al. disclose similar imidazole/phenyl compounds as the instant invention. Accordingly, unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Furthermore, even if unity of invention under 37 CFR 1.475(a) is not lacking, which it is lacking, under 37 CFR 1.475(b) a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations:

(1) A product and a process specially adapted for the manufacture of said product', or

(2) A product and a process of use of said product; or

(3) A product, a process specially adapted for the manufacture of the said product, and a use of the said product; or

(4) A process and an apparatus or means specifically designed for carrying out the said process; or

(5) A product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process.

And, according to 37 CFR 1.475(c)

if an application contains claims to more or less than one of the combinations of categories of invention set forth in paragraph (b), unity of invention might not be present.

However, it is noted that unity of invention is considered lacking under 37 CFR 1.475(a) and (b). Therefore, since the claims are drawn to more than a product, and according to 37 CFR 1.475 (e)

> the determination whether a group of inventions is so linked as to form a single general inventive concept shall be made without regard to whether the inventions are claimed in separate claims or as alternatives within a single claim.

The claims lack unity of invention and should be limited to only a product, or a process for the preparation, or a use of the said product. In the instant case, Groups I-III are drawn to various products, processes of making, and the final products do not contain a common technical feature or structure, and do not define a contribution over the prior art, i.e., similar compounds having aryl or heteroaryl (i.e., imidazole) moiety. Moreover, the examiner must perform a commercial database search on the subject matter of each group in addition to a paper search, which is quite burdensome to the examiner.

Claims 42-62, in part, embraced in above elected subject matter, are prosecuted in the case. Claims 42-62, in part, not embraced in above elected subject matter, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

The requirement is still deemed proper and therefore made FINAL.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 59-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling compounds of formula (I) for treating pain, does not reasonably provide enablement of compounds of formula (I) for treating or preventing diseases mediated by cyclooxygenase-2, see claim 59. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 59-62 are drawn to intent methods of use using compounds of formula (I) for treating or preventing diseases without limitation (i.e., no named diseases).

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face. McClure et al. US 6,696,464 disclose similar cyclooxygenase inhibitor for treating pain or arthritis.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming intent methods of use using compounds of formula (I) for treating or preventing diseases without limitation (i.e., no named diseases). As such, the specification fails to enable the skilled artisan to use the compounds of claims effective to "treat or prevent diseases" without limitation (i.e., no named diseases).

In addition, there is no established correlation between *in vitro* or in *vivo* activity and accomplishing treatment or prevention of "diseases" without limitation (i.e., no named diseases), and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use compounds of formula (**I**) since there is no description of an actual method wherein "treating or preventing diseases" without limitation in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds of formula (**I**) due to the unpredictability of the "treating or preventing diseases" without limitation (i.e., no named diseases). The "treating or preventing diseases" without limitation (i.e., no named diseases) is known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of

Animal model for treating pain or inflanmmation, see pages 28-30 of the specification. There are no *in vitro* or *in vivo* working examples present for the treatment or prevention diseases without limitation by the administration of the instant invention.

The breadth of the claims

The breadth of the claims is methods of use of the instant compounds effective to "treating cancer" without limitation (i.e., no named cancer).

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what "treating or preventing diseases" without limitation would be benefited (i.e., treated or prevented) by the administration of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment or prevention of a disease, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims for the "treating cancer" without limitation.

As a result necessitating one of skill to perform an exhaustive search for which "treating or preventing diseases" without limitation, can be treated by what pharmaceutical compounds of the instant claims in order to practice the claimed invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds in regards to the treatment of the many diseases resulting from "modulating SIP receptors" without limitation, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by deletion the limitation "prevention" and incorporation of the named diseases (i.e., see claim 62, diseases related to inflammation only) into claim 59 would obviate the rejection.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Chakravarty et al. CAS: 120:45975.

Applicants claim compounds o formula (I), see claim 42.

Chakravarty et al. disclose a compound, see RN: 150589-21-2. It clearly anticipates the instant compounds of formula (I), wherein the variable R1 represents phenyl-alkyl, the variable D represents phenyl, the variable A represents an unsaturated 6-memnber ring (i.e., phenyl), and the variable L is a bond, and the variable B represents substituted heteroaryl. Dependent claims 43-62 are also rejected along with claim 42 under 35 U.S.C. 102(b).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.

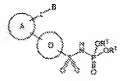
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chakravarty et al. US 5,162,340.

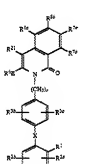
Applicants claim compounds/compositions of formula (I), i.e.,



, wherein the variable D represents phenyl, the variable A represents an unsaturated 6-memnber ring (i.e., phenyl), and the variable L is a bond, and the variable B represents substituted heteroaryl, see claim 42.

Determination of the scope and content of the prior art (MPEP §2141.01)

Chakravarty et al. discloses compounds/compositions of formula (I), i.e.,



, wherein the variables R1 represents  , and R24 represents alkoxy, see columns 2-7.

Determination of the difference between the prior art and the claims (MPEP §2141.02)

The difference between instant claims and Chakravarty et al. is that the instant variable A represents an unsaturated 6-memnber ring (i.e., phenyl) or imidazole, while Chakravarty et al. represents an unsaturated 6-memnber ring (i.e., phenyl) at the same position. Chakravarty et al. compounds inherently overlap with the instant invention.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims 42-62 prima facie obvious because one would be motivated to employ the compounds of Chakravarty et al. to obtain instant compounds of formula (I), wherein the variable D represents phenyl, the variable A represents an unsaturated 6-memnber ring (i.e., phenyl), and the variable L is a bond, and the variable B represents substituted heteroaryl. Dependent claims 43-62 are also rejected along with claim 42 under 35 U.S.C. 103(a).

The motivation to make the claimed compounds derived from the known compounds of Chakravarty et al. would possess similar activity (i.e., composition) to that which is claimed in the reference.

Claims Objection

8. Claims 42-62 are objected to as containing non-elected subject matter, i.e., heterocyclic or heteroaryl , thiazole, 2,5-dihydrofuran, thiophene, pyridine, 4H-pyran, etc. It is suggested that applicants amend the claims to the scope of the elected subject matter as defined on the pages 2-3 *supra*.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph

K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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September 03, 2008